Treatment outcomes and associations in an adolescent specific early intervention for psychosis service

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Abstract

Compared with adult onset psychosis, adolescent psychosis has been associated with poorer outcomes in terms of social and cognitive functioning and negative symptoms (Boeing et al., 2007; Mayoral et al., 2008). Young people experiencing first episode psychosis have developmental needs that frequently pre-date and are compounded by psychosis onset (Gumley & Schwannauer, 2006; Harrop & Trower, 2001). There is a lack of published studies of adolescent onset psychosis and further information is needed so that developmentally appropriate interventions can be developed (Schimmelmann & Schultze-Lutter, 2012).

We report an observational naturalistic cohort study of an adolescent specific service, the Early Psychosis Support service (EPSS). We examined baseline demographic and clinical variables, treatments outcomes, and predictors of outcome for this population. The mean age of our sample was 16.3 years. Median duration of untreated illness (DUI) was 88 weeks, and median duration of untreated psychosis (DUP) was 16 weeks. We found significant improvements in positive symptoms, negative symptoms, disorganisation, excitement, emotional distress and depression from 0 to 12 months. We found that baseline positive symptoms and DUI significantly predicted positive symptoms at 12 months and only negative symptoms at baseline predicted 12-month negative symptoms.

Our finding that specialist early intervention for adolescents experiencing psychosis is effective suggests that such treatment should be routinely offered in line with existing clinical guidelines. Our finding that DUI is predictive of poorer outcome at 12 months suggests that even earlier intervention from a specialist team may further improve treatment outcomes.

Introduction

Adolescence is a developmental period with vulnerabilities and opportunities which impact on a young person's social world. We follow Sawyet et al (DATE) in defining this life phase as occurring between the ages of 10 and 24 years. Psychosis during adolescence can disrupt normal adolescent processes and place young people at a disadvantage in developing identity and independence (Gumley & Schwannauer, 2006; Harrop & Trower, 2001). For example, inpatient admissions can disrupt education, and effects of medication treatments such as weight gain, cognitive slowing and sexual dysfunction may hamper confidence in peer relationships. Onset of psychosis in adolescence is associated with more severe positive and negative symptoms, poorer premorbid functioning, higher suicidality and longer duration of untreated psychosis (DUP) i.e. the period between the onset of psychosis to the commencement of treatment (Armando et al., 2015; Dominguez et al., 2013; Frazier et al., 2007; Joa et al., 2008; Schimmelmann, Conus, Cotton, McGorry, & Lambert, 2007). Delays to appropriate treatment may leave adolescents vulnerable to negative social outcomes such as increased isolation and self-stigma.

A recent meta-analysis highlighted a lack of research investigating treatment efficacy for adolescent psychosis (Stafford et al., 2015). Psychological treatments remain largely untested in adolescent populations, despite findings of their effectiveness with adults. Anti-psychotic medication had only small beneficial effects in treating psychotic symptoms (SMD=-0.42) but medium adverse effects on weight gain (WMD=1.61) and discontinuation due to side effects (RR=2.44) (Stafford et al., 2015). The balance of costs to benefits of anti-psychotic medication in young people suggests that caution in prescribing is warranted, despite current UK clinical guidelines advising anti-psychotic medication as a first line treatment (NICE, 2013; Stafford et al., 2015). Current clinical guidelines recommend multi-disciplinary team-based early intervention for psychosis based on the 'critical period hypothesis'((SIGN), 2013; Birchwood, Todd, & Jackson, 1998; NICE, 2013). Early intervention has been repeatedly found to be effective in treating first episode psychosis e.g. insert Corell & Nordentoft refs(Norman et al., 2011) however there is little evidence for its efficacy in treating adolescent psychosis specifically.

Two dimensions of untreated difficulty have received attention in the literature: Duration of untreated illness (DUI) refers to the time between first noticeable mental state changes and commencement of treatment and duration of untreated psychosis (DUP) refers to the time between the onset of clinically significant psychotic symptoms and appropriate treatment.

The concept of DUI has allowed observation of untreated illness in people who experience psychosis beyond psychosis itself, and extended the concept of untreated illness to a range of psychiatric diagnoses (Dell'Osso & Altamura, 2010), taking into account the lack of diagnostic specificity in early onset psychosis. However, there is a lack of a clearly agreed definition of DUI with consensus cut-offs and this may account for wide variance in average DUI ratings (Altamura et al., 2018; Dell'Osso & Altamura, 2010). Measurement of DUP has more clearly defined parameters and is widely used in psychosis research (Murru & Carpiniello, 2016).

Numerous studies have established associations between treatment delays and outcome in first-episode psychosis. Extended DUI has been related to greater adversity, living alone, unemployment and more threatening and bizarre behaviour at service entry (Owens, Johnstone, Miller, Macmillan, & Crow, 2010). It has also been associated with worse outcome in those diagnosed with bipolar disorder (Altamura et al., 2018) and psychosis (Malla et al., 2006). Longer DUP is associated with poorer long-term symptomatic and functional outcomes in first episode psychosis (Boonstra et al., 2012; Hill et al., 2012; Marshall et al., 2005; Perkins, 2006). In adolescent psychosis, long DUP has been associated with subsequent global functioning and executive functioning difficulties (Fraguas, del Rey-Mejias, et al., 2014) and lower pre-morbid social functioning has been associated with more severe negative symptoms and poorer social functioning at 12 months (Meng et al., 2006). Recent studies have found that DUP is related to individual and service factors such as age, cannabis-use, delayed help-seeking and referral route (Bechard-Evans et al., 2007; Cratsley, Regan, McAllister, Simic, & Aitchison, 2008; Dominguez et al., 2013; Fond et al., 2017). There is evidence to suggest that interventions aimed at reducing DUP may be less effective for adolescent populations, unless they have a specific youth pathway (Birchwood et al., 2013; Chan et al., 2016). A recent meta-analysis highlighted difficulty reducing DUP in first episode psychosis (FEP) finding no evidence for the efficacy of current interventions in FEP (Oliver et al., 2018). There was evidence for DUP reduction in clinical high-risk services, suggesting that developmentally appropriate preventative strategies may be a viable and effective option (Oliver et al., 2018).

Overall, the existing literature suggests that DUI and DUP may reflect psychological and interpersonal processes leading to worse outcomes, as well as contextual factors such as service accessibility. There is relatively little information for adolescent psychosis specifically.

Aims

An observational cohort study of an adolescent specific Early Psychosis Support Service (EPSS). We aim to describe the young people accessing the service in terms of their demographic and clinical characteristics, examine treatment outcomes, and predictors of outcome. Ethical approval (17/SS/0116) was granted on 6TH November 2017.

Method

Service

EPSS accepts referrals for young people aged 13 to 18 years experiencing a first episode or an ultra high-risk mental state for psychosis. EPSS works with individuals for up to three years using an early intervention approach recommended in Scottish Intercollegiate Guidelines Network (SIGN) guidelines consisting of: engagement/assertive outreach approaches, family involvement and interventions, psychological interventions and psychologically informed care, vocational/educational interventions and access to antipsychotic medication ((SIGN), 2013). Key-worker's caseloads are capped at 15 young people to allow sustained outreach work and additional contacts during crisis where necessary. The service routinely assesses symptoms of psychosis and depression and psychological adaption to evaluate and inform clinical intervention. Frequency of contacts varies depending on the needs of the young person. The service emphasizes the importance of emotional and social recovery from psychosis but also ensures that young people have access to antipsychotic medication as necessary. Early treatment with EPSS focuses on stabilization, engagement and therapeutic relationship building. The multi-disciplinary team was trained in adaptive mentalization-based integrative treatment (AMBIT) in 2011 and now uses this approach in routine team working with young people (Bevington, Fuggle, Fonagy, Target, & Asen, 2013) in order to maximise the chances of effective engagement. Once young people are engaged in the service further therapeutic treatments such as family work and occupational therapy are offered. Psychological therapy is offered using a cognitive interpersonal approach to staying well after psychosis (Gumley & Schwannauer, 2006).

Participants

Basic demographic and health service use data was collated for young people attending the service between May 2005 and August 2017. In addition, young people were administered the positive and negative syndrome scale (PANSS) and Beck Depression Inventory (BDI-II) as outcome measures for clinical and evaluation purposes.

Measures

Help-seeking and Delays to Treatment

All measurements relating to help-seeking and delays to treatment were gathered through thorough examination of case notes by the Assistant Psychologist in the team. DUI, DUP and number of help-seeking attempts were represented visually on a timeline for each young person. Definitions for DUI, DUP and help-seeking were taken from the work of Norman and colleagues (Norman, Malla, Verdi, Hassall, & Fazekas, 2004). Timelines contained information relating to onset of symptoms, functioning, contact with health and social services and significant social events. These were discussed by the MDT in formulations and in supervision with the Consultant Clinical Psychologists in the team (H.G. & M.S.), to provide consensus ratings.

Duration of untreated illness (DUI) was defined as the onset of "noticeable psychiatric symptoms, such as marked symptoms of depression or anxiety" and/or the first signs or symptoms that indicate a change from an individual's previous level of functioning (Norman, Malla, Verdi, Hassall, & Fazekas, 2004). Duration of untreated psychosis was calculated as the date from the onset of psychosis to the onset of criteria treatment (Norman, Malla, Verdi, Hassall, & Fazekas, 2004). Onset of psychosis was based on a consensus estimate of the date when any one positive symptom on the PANSS was rated as moderate or above in the context of a manifestation of psychotic symptoms and lasted throughout the day for several days or several times a week or a cluster of positive symptoms reaching a total rating of 7 or more including at least one of delusions, conceptual disorganization or hallucinatory behaviour. Onset of criteria treatment was the date in which neuroleptic treatment at recommended dosage levels was commenced and continued for a period of at least a month or led to a significant reduction in symptoms. Alternatively, engagement with the specialist EPSS service was considered as an onset of criteria treatment. Help-seeking was defined as the act of seeking advice/treatment from an external individual or agency who could be reasonably construed to be a 'helping professional'.

Clinical Assessment

The Positive and Negative Syndrome Scale (PANSS) was used to measure symptom severity at 0 and 12 months (Kay, Flszbein, & Opfer, 1987; Kay, Opler, & Lindenmayer, 1989). Ratings were based on responses to a clinical interview, reports from staff and carers and clinical case notes. The PANSS was scored using a five-factor structure of the following symptom subscales: positive symptoms, negative symptoms, excitation, emotional distress and disorganization

(Lancon, Aghababian, Llorca, & Auquier, 1998; Lancon, Auquier, Nayt, & Reine, 2000). The Beck Depression Inventory (BDI-II) was used to assess self-reported symptoms of depression (Beck, Steer, Ball, & Ranieri, 1996; Beck, Steer, & Brown, 1996).

Data Analysis

All analyses were specified 'A priori' in a data analysis plan agreed at the outset. Data was analysed using IBM SPSS v.23. Alongside basic descriptive statistics, we proposed paired t-tests to examine differences in clinical variables at entry to the service and 12 months in service. We proposed sequential multiple regressions to examine the effects of DUI, DUP and help-seeking on clinical outcomes at 12 months. Baseline symptoms for that subscale were entered in the regression model followed by DUI, DUP, help-seeking for all PANSS subscales and the BDI-II. All variables were examined for accuracy of data entry, missing values, and assumptions of multivariate analysis. These results led to log transformation of variables to reduce skew. With $p<0.001$ criterion for Mahalanobis distance, no multivariate outliers were identified.

Missing Data

Due to the naturalistic nature of this cohort study over a 10 year period in an active clinical service, there was a high proportion of missing data. To assess the extent to which individual factors may influence missing data, chi-squared and t- tests were run to examine group differences between those with available 12-month PANSS data and those without. This revealed no significant effect of gender ($X^2(1)=0.074$, $p=0.79$), DUI ($t=0.061$, $p=0.951$) or DUP ($t=-0.329$, $p=0.743$) on missing data. Those with missing 12-month PANSS data were significantly younger than those with complete 12-month PANSS data ($t=-2.66$, $p=0.009$). To control for the potential effect of age on 12-month predictors of outcome, age was entered as an initial predictor in multiple regression analyses. Age did not significantly predict 12-month PANSS scores for positive symptoms ($R^2=0.006$, $R=0.076$, $F=0.174$, $p=0.679$), negative symptoms ($R^2=0.066$, $R=0.258$, $F=2.419$, $p=0.129$), excitement ($R^2=0.001$, $R=0.035$, $F=0.043$, $p=0.836$), emotional distress ($R^2=0.019$, $R=0.137$, $F=0.667$, $p=0.420$) or disorganisation ($R^2=0.000$, $R=0.002$, $F=0.000$, $p=0.992$). Therefore, age was removed as a predictor in the final analysis. Missing data was excluded listwise in subsequent analyses.

Results

Basic demographic and clinical characteristics

Table 1 displays the demographic characteristics of the sample upon entry to the service.

Table 1: Basic demographic characteristics

Table 2 displays clinical characteristics at baseline. The median number of help-seeking attempts was 1 (range: 1-8) and 66 (52%) individuals had contact with services prior to their first contact with the EPSS service. The median duration of untreated illness (DUI) was 88 weeks; median duration of untreated psychosis (DUP) was 16 weeks replicating the findings of (Gumley et al., 2014) in a slightly older cohort (mean age = 24.64 years). The observed DUP is longer than similar studies describing adolescent cohorts e.g. (Fraguas et al. 2014, Meng et al. 2006). Forty four (34.9%) young people had untreated psychosis whilst in contact with mental health services. 39 (29.1%) were admitted to the inpatient unit on first contact and 22 (16.4) were treated under the mental health act. In terms of symptomology, this sample scored comparatively on the PANSS for positive and negative symptoms as the adolescent sample of Meng et al. (2006).

Table 2: Basic clinical characteristics

Treatment outcomes

Table 3 demonstrates comparative 12-month clinical outcomes. Symptomatic improvement reached statistical significance across all measured domains on the PANSS interview and BDI questionnaire. There were large effect sizes for positive symptoms ($t=5.81$, $p<0.001$, $d=1.07$), excitement ($t=5.84$, $p<0.001$, $d=1.09$) and emotional distress ($t=6.18$, $p<0.001$, $d=0.94$), a medium effect for symptoms of disorganisation ($t=3.59$, $p=0.001$, $d=0.57$), and small-medium effects for negative symptoms ($t=3.28$, $p=0.002$, $d=0.46$) and depression ($t=2.81$, $p=0.008$, $d=0.46$).

Table 3: 12 month clinical outcomes

Predictors of outcome

For PANSS positive symptoms at 12 months, the overall regression model of treatment delay and help seeking attempts accounted for 27% of the variance ($R^2=0.27$ Adjusted $R^2=0.162$, $R=0.519$, $F=2.5$). The significant predictor variables were positive symptoms at baseline and DUI. The regression model for negative symptoms accounted for 42% of the variance at 12 months ($R^2=0.42$, Adjusted $R^2=0.34$, $R=0.65$,$F=5.57$). Negative symptoms at baseline were the only significant predictor, and DUI was non-significant ($p=0.07$). In terms of emotional distress, the model predicted 38% variance with baseline symptoms and DUI as significant predictors ($R^2=0.38$, Adjusted $R^2=0.31$, $R=0.62$, $F=5.0$). In contrast, self-reported symptoms of depression as measured on the BDI were significantly predicted by baseline depression with DUP approaching significance ($p=0.06$). DUI was not a significant predictor for depression at 12

months. The overall model for depression accounted for 55% of the variance in 12-month depression scores (R^2=0.55, Adjusted R^2=0.45, R=0.74 , F=5.2).

Table 4 Predictors of 12-month outcome

Discussion

We described a cohort of adolescents attending an adolescent the Early Psychosis Support Service (EPSS) and examined whether specialist treatment for psychosis was effective in this population. We found statistically significant improvements across all symptomatic domains concluding that early intervention is effective for adolescent psychosis. Significant improvements were observed not just in relation to positive symptoms, but also for negative symptoms and distress, despite reports of the relative treatment resistance of negative symptoms and depression in this population. Previous research has suggested that adolescent psychosis may be particularly difficult to treat with adolescent onset typically associated with poorer longer-term outcomes than adult onset psychosis (Frazier et al., 2007; Hui et al., 2014; Veru, Jordan, Joober, Malla, & Iyer, 2016). However, we found that developmentally appropriate care provided by a multi-disciplinary team focussing on social, emotional and vocational recovery was effective in treating adolescent psychosis. Similarly, negative symptoms have been previously found to be more difficult to treat than psychosis, particularly with anti-psychotic medication (Aleman et al., 2017). Recent meta-analyses have found that specific psychological treatments with a focus on social recovery (e.g. social skills based training) are effective in treating negative symptoms (Lutgens, Gariepy, & Malla, 2017; Turner et al., 2017). Our finding that negative symptoms improved over the first 12-months of treatment can be understood within the EPSS treatment emphasis on social and emotional recovery.

A second aim of our study was to investigate the relationship between treatment delays and help-seeking characteristics and later outcomes. We found that DUI but not DUP was a significant predictor of outcome for positive symptoms and emotional distress and approached significance for negative symptoms; this is indicative of the lack of specificity in the prodromal development of adolescent onset psychosis. Previous studies have highlighted that DUP is not consistently predictive of outcome for adolescents e.g. (Fraguas, Merchán-Naranjo, et al., 2014; Meng et al., 2006). Developmental processes may, in part, contribute to treatment delays and increased vulnerability for some individuals. We previously reported an over-representation of insecure attachment, especially dismissing and unresolved trauma, in first-episode psychosis (Gumley et al., 2014; Gumley, Taylor, Schwannauer, & MacBeth, 2013). Studies have also identified associations between metacognition, social functioning, service engagement and symptoms suggesting that people who have social difficulties and difficulties understanding others minds may also be less able to engage with treatment effectively (Macbeth et al., 2014; McLeod, Gumley, Macbeth, Schwannauer, & Lysaker, 2014; Meng et al., 2006).

Once engaged with services, such vulnerabilities represent modifiable qualities of interactions and relationships between individuals, families and services. Recently, there has been interest

in designing accessible services for young people who have historically been considered 'hard to reach' by services. Approaches such as the AMBIT (adolescent mentalization based integrative therapy) which uses team-based techniques and strategies to facilitate a mentalizing environment where individuals can begin to develop a sense of being known in mental state terms, have been found effective in treating adolescent populations with high levels of psychopathology and distress (Bevington, Fuggle, & Fonagy, 2015; Bevington et al., 2013; Griffiths, Noble, Duffy, & Schwannauer, 2017).

Our finding that baseline negative symptoms predicted 30% variance in negative symptoms at 12 months is in line with previous studies which have found early negative symptoms to be a robust predictor of outcome in adolescent psychosis (Díaz-Caneja et al., 2015). Studies focusing on attachment in first-episode psychosis have found that a dismissing attachment style is related to negative symptoms, suggesting that negative symptoms are related to down-regulating tendencies in managing emotion (Gumley et al. 2014). Mentalization and metacognition difficulties have also been associated with negative symptoms (Macbeth et al., 2014; Weijers et al., 2018). It is possible that individuals with pre-existing difficulties in understanding their social world are vulnerable to a process of social withdrawal already present at the point of first contact with services. It is important to note that processes maintaining negative symptoms are not absolutely determined; we found symptomatic improvement in negative symptoms over a relatively short time period in our sample. It may be that the service emphasis on social and emotional recovery treatment helped to improve motivation and social engagement.

We found that baseline emotional distress and DUI predicted distress at 12 months as measured on the PANSS interview. In contrast, only baseline depression predicted later depression when using the BDI self-report measure, though DUP approached significance as a predictor. It is possible that these findings represent distinct pathways to depression in first episode psychosis, perhaps representing long-standing low mood and distress, or a period of low mood following a psychotic episode (Birchwood, 2003; Upthegrove, Marwaha, & Birchwood, 2017)

Limitations

This study consists of data collected from an active clinical service over a ten-year period. Our sample was relatively small, potentially leading to null findings through inadequate power. In common with other studies that rely on routinely collected outcome data from clinical services, there were problems with missing data. Data in the service was collected by members of the multidisciplinary clinical team supported by an assistant psychologist. Data collection was likely to have been compromised by factors such as service user lack of engagement and attrition, staff's prioritisation of clinical needs, staff reluctance to administer outcome measures when they consider an individual to be too unwell, and staff turnover leading to training needs in the relevant assessment tools. Trends in the missing data could limit the interpretability of findings. For example, the average age of participants with missing 12-months PANSS scores was younger than those with complete 12-month scores thus creating bias in our sample. We addressed this by controlling for age in our multiple regression analysis finding no significant effect of age on 12-month PANSS scores. It is possible, however,

that had there been more available data for younger individuals, that age may have exhibited an effect on outcome.

Following the guidance of Norman et al (2004), we used a definition of DUP in our study whereby commencement of treatment could be referral to the specialist EPSS team or commencement of an antipsychotic. Recently researchers have sought to apply stricter definitions to DUP separating DUP1 (initiation of antipsychotic medication) and DUP2 (enrolment in in an EI service) (Golay et al. Insert ref). Such differentiation may give the DUP concept more precision in the future.

Our limitations highlight some of the challenges faced in providing a high quality and equitable service for adolescents experiencing psychosis. Our finding that DUI predicts poor outcome at 12 month suggests that there are a number of individuals not accessing treatment when it is needed.

Clinical Implications

We found that developmentally appropriate specialist early intervention is effective in treating adolescent psychosis. A key challenge for services is to reduce the time-to-treatment for adolescents experiencing psychosis (Ballageer, Malla, Manchanda, Takhar, & Haricharan, 2005; Birchwood et al., 2013). Our findings suggest that delays accessing appropriate treatment indicate vulnerability to experiencing later difficulties over a 12-month period. This may, in part, be related to individual's help-seeking tendencies, but also implicates a key avenue for services to engage young people who may struggle to ask for help. Specific youth pathways and service models may be useful (Birnbaum, Candan, Libby, Pascucci, & Kane, 2016).

Our findings suggest that adolescents with psychosis, including those who are socially withdrawn, have the capacity for change and recovery over a relatively short time period. Although greater psychopathology and reduced help-seeking tends to predict greater chronicity and ongoing difficulty, our findings suggest that this is not by any means a given, nor some inherent individual characteristic. Developmentally appropriate multi-faceted care encompassing psychological and family work, access to social support and medication as an option improves outcomes for adolescent psychosis. It is likely that such an approach is effective through building trust and understanding between young people and their social networks.

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Table 1:

Demographic Variable	**N=141**
Age, mean (SD), years	16.13 (1.35)
[95% CI]	[15.9 - 16.35]
Sex, no. (%)	
Male	80 (56.7)
Female	61 (43.3)
Ethnicity/Nationality, no. (%)	**N=137**
White British	118 (86.13)
Other	19 (13.87)
Education level, no. (%)	**N=127**

Left school before 16	14 (9.9)
Left school at 16	30 (21.3)
Left school 17-18	18 (12.8)
Still in school	64 (45.4)
Did not complete College	1 (0.7)
Occupation at entry to service, no. (%)	**N=128**
Student	83 (64.8)
Unemployed	37 (28.91)
Full time work (paid)	3 (2.1)
Part time work (paid)	5 (3.5)
Residence at entry to service, no. (%)	**N=128**
Family home	111 (86.7)
Rented accommodation	7 (5.5)
Other	10 (7.8)

Table 2:

Clinical Variable		**N**
DUI, median (range), weeks	88 (575)	91
DUP, median (range), weeks	16(252)	91
No. helpseeking attempts, median (range)	1 (8)	111
Previous contact with mental health services, no., %		127
Yes	61 (48)	
No	66 (52)	
Admitted at first contact no., %		134
Yes	39 (29.1)	
No	95 (70.9)	
CTO first contact no., %		134
Yes	22 (16.4)	
No	112 (83.6)	
DUP in service no., %		126
Yes	44 (34.9)	
No	82 (65.1)	
Positive symptoms, mean (SD)	23.05 (7.28)	76
[95% CI]	[21.39 - 24.72]	
Negative symptoms, mean (SD)	21.28 (8.60)	89
[95% CI]	[19.37 - 23.00]	
Excitement, mean (SD)	17.14 (6.43)	92
[95% CI]	[15.81 - 18.47]	
Emo distress, mean (SD)	20.75 (6.90)	93
[95% CI]	[19.34 - 22.17]	
Disorganisation, mean (SD)	18.8 (7.75)	75
[95% CI]	[17.02 - 20.58]	
BDI-II, mean (SD)	23.62 (15.12)	100
[95% CI]	[20.62 - 26.62]	

Table 3:

	N	t	Cohen's d	p
Positive symptoms	47	5.81	1.07	<0.001
Negative symptoms	54	3.28	0.46	0.002
Disorganisation	47	3.59	0.57	0.001
Excitement	56	5.84	1.09	<0.001
Emotional distress	55	6.18	0.94	<0.001
BDI-2	34	2.81	0.46	0.008

Table 4:

Positive symptoms	**B**	**SE B**	**Beta**	**95% CI for B (lower)**	**95% CI for B (upper)**	**sr^2 (incremental)**	**Sig F change**
Positive symptoms baseline	0.39	0.20	0.33	-0.03	0.81	0.12	0.05
DUI (log)	0.10	0.05	0.34	-0.01	0.20	0.15	0.02
DUP (log)	0.02	0.06	0.07	-0.11	0.15	0.00	0.71
HS (log)	0.00	0.21	0.00	-0.43	0.44	0.00	0.99
R^2=0.27 Adjusted R^2=0.162, R=0.519, F=2.5							
Negative symptoms							
Negative symptoms baseline	0.63	0.18	0.49	0.26	0.99	0.30	0.00
DUI (log)	0.05	0.05	0.19	-0.04	0.15	0.07	0.07
DUP (log)	0.00	0.05	0.00	-0.11	0.11	0.01	0.60
HS (log)	0.23	0.16	0.23	-0.09	0.55	0.04	0.15
R^2=0.42, Adjusted R^2=0.34, R=0.65 ,F=5.57							
Excitement							
Excitement baseline	0.15	0.18	0.16	-0.22	0.52	0.09	0.06
DUI (log)	0.02	0.04	0.09	-0.06	0.10	0.04	0.19
DUP (log)	0.03	0.04	0.16	-0.06	0.12	0.02	0.33
HS (log)	0.11	0.14	0.16	-0.18	0.40	0.02	0.43
R^2= 0.18, Adjusted R^2=0.08, R=0.42 , F=1.77							
Emotional Distress							
Emo Distress baseline (log)	0.49	0.17	0.41	0.14	0.83	0.22	0.00
DUI (log)	0.07	0.05	0.27	-0.02	0.17	0.13	0.01
DUP (log)	0.05	0.05	0.17	-0.05	0.15	0.03	0.24
HS (log)	0.04	0.16	0.04	-0.28	0.36	0.00	0.79
R^2=0.38, Adjusted R^2=0.31, R=0.62 , F=5.0							
Disorganisation							
Disorganisation baseline (log)	0.37	0.16	0.42	0.04	0.70	0.22	0.01
DUI (log)	0.06	0.04	0.28	-0.02	0.15	0.09	0.07
DUP (log)	-0.02	0.05	-0.06	-0.12	0.09	0.00	0.99
HS (log)	0.13	0.18	0.15	-0.24	0.51	0.01	0.48
R^2=0.32, Adjusted R^2=0.21, R=0.56 , F=3.11							
BDI 2							
BDI baseline (log)	0.77	0.24	0.56	0.27	1.27	0.40	0.00
DUI (log)	-0.09	0.13	-0.14	-0.36	0.18	0.00	0.74
DUP (log)	0.22	0.12	0.34	-0.04	0.48	0.11	0.06
HS (log)	0.59	0.51	0.20	-0.49	1.67	0.04	0.26
R^2=0.55, Adjusted R^2=0.45, R=0.74 , F=5.2							